

Fig. 1

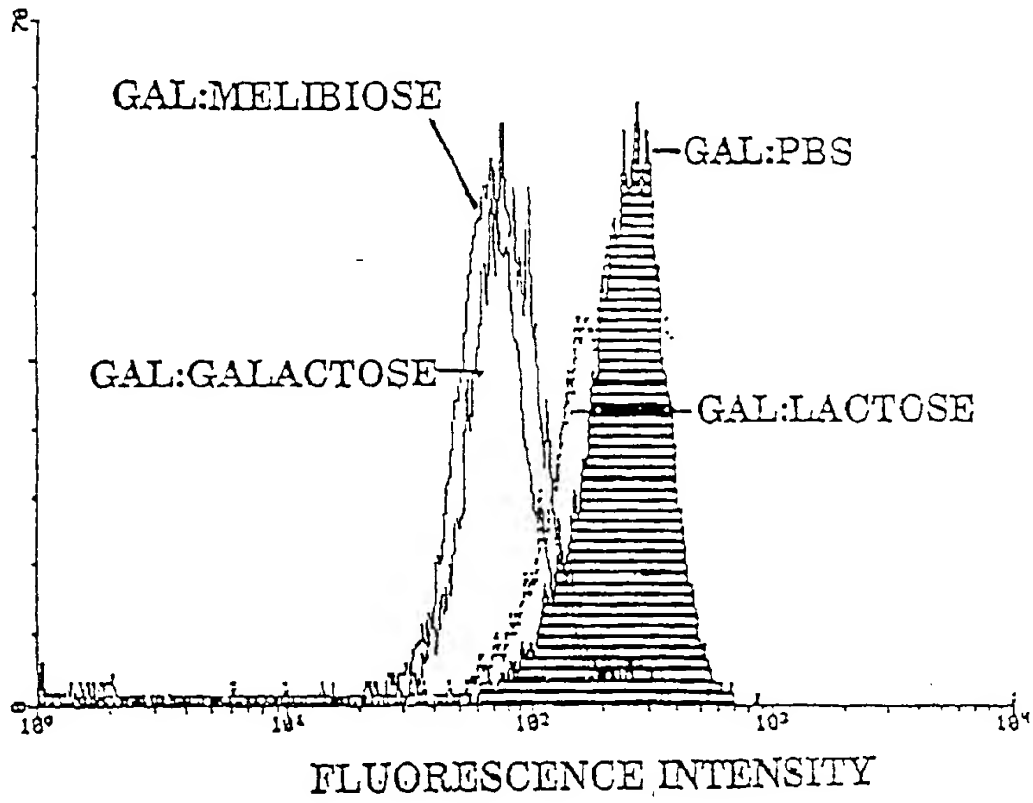


FIGURE 2

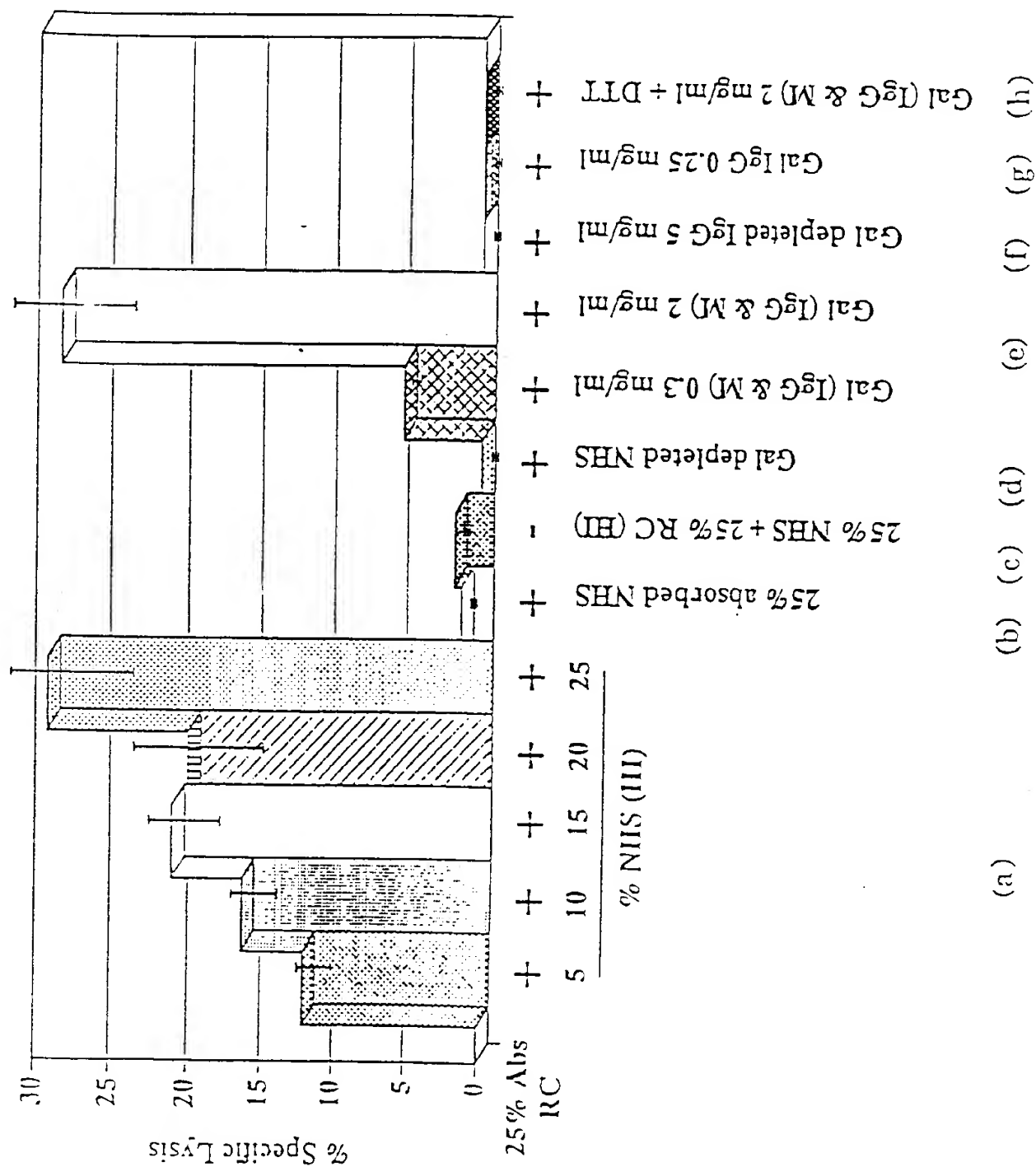
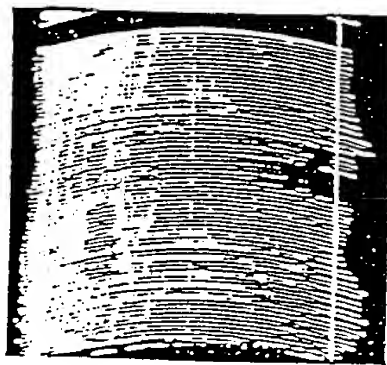


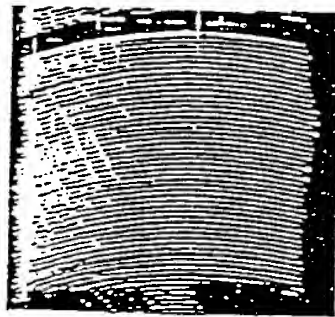
FIGURE 3



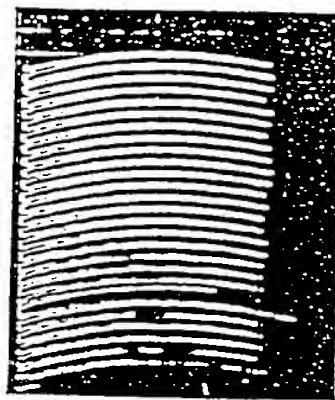
Baseline



10mM Melibiose



5 % plasma



13 % plasma

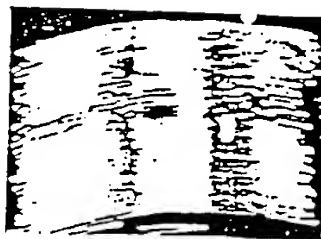


Fig 1
 FOR Line-up (nt):

PCTCD	1	-----	-----	-----	-----	50
DOVGSTA	1	CGCGCGCGCG	CGCGCGCGCG	CGCGCGCGCG	CGCGCGCGCG	50
MUSGLYTNB	1	-----	-----	-----	-----	50
PCTCD	51	-----	-----	-----	-----	100
DOVGSTA	51	CGCGCGCGCG	CGCGCGCGCG	CGCGCGCGCG	CGCGCGCGCG	100
MUSGLYTNB	51	-----	-----	-----	-----	100
PCTCD	101	-----	-----	-----	-----	150
DOVGSTA	101	CGCGCGCGCG	CGCGCGCGCG	CGCGCGCGCG	CGCGCGCGCG	150
MUSGLYTNB	101	-----	-----	-----	-----	150
PCTCD	151	-----	-----	-----	-----	200
DOVGSTA	151	CGCGCGCGCG	CGCGCGCGCG	CGCGCGCGCG	CGCGCGCGCG	200
MUSGLYTNB	151	-----	-----	-----	-----	200
PCTCD	201	-----	-----	-----	-----	250
DOVGSTA	201	CGCGCGCGCG	CGCGCGCGCG	CGCGCGCGCG	CGCGCGCGCG	250
MUSGLYTNB	201	-----	-----	-----	-----	250
PCTCD	251	-----	-----	-----	-----	300
DOVGSTA	251	CGCGCGCGCG	CGCGCGCGCG	CGCGCGCGCG	CGCGCGCGCG	300
MUSGLYTNB	251	-----	-----	-----	-----	300
PCTCD	301	-----	-----	-----	-----	350
DOVGSTA	301	CGCGCGCGCG	CGCGCGCGCG	CGCGCGCGCG	CGCGCGCGCG	350
MUSGLYTNB	301	-----	-----	-----	-----	350
PCTCD	351	-----	-----	-----	-----	400
DOVGSTA	351	CGCGCGCGCG	CGCGCGCGCG	CGCGCGCGCG	CGCGCGCGCG	400
MUSGLYTNB	351	-----	-----	-----	-----	400
PCTCD	401	AGAGCTCACT	AGAACTT-CT	TTT----GCG	TTTTACTCTG	450
DOVGSTA	401	CGAGCTCACT	AGAACTT-GG	TACTTTTGGC	TTTTACTCTA	450
MUSGLYTNB	401	AGAGCTCACT	AGAACTTGG	TTGCTTTGCT	TTTTGCTTTG	450
PCTCD	451	AGCAGACCAT	CAG-----	-----	-----	500
DOVGSTA	451	AGCAGACCAT	CAG-----	-----	-----	500
MUSGLYTNB	451	AGCTCACCAT	CAGCTCACT	TTCAACTCAA	CAGATCTGCT	500
PCTCD	501	-----	-----	-----	-----	550
DOVGSTA	501	-----	-----	-----	-----	550
MUSGLYTNB	501	TCTTGGAACT	AAAGCCCTCT	ACTACCTTCC	CTGGACCTAA	550
PCTCD	551	-----	-----	-----	-----	600
DOVGSTA	551	-----	-----	-----	-----	600
MUSGLYTNB	551	ATCACTATOC	TTCAAGATCT	CGATCTCAAC	AAATCTTCCA	600

Exn 1 Exn 2

Exn 2 Exn 3

Fig 4 (cont) 4-2

			Exon 3 ↓ Exon 4	
PGTCD	601	-----	-----	650
BOVGSTA	601	-----	-----	650
MUSGLYTNS	601	CAAGTCAGAA	ACAAGTCTTC CATCCTCAAC ATCTCGATCA CAGCAGAAA	650
		STAAT		
PGTCD	651	TAATCAATCT	CAAGCAAGA CTGCTTCTCT CAATGCTGCT TGTCTCAACT	700
BOVGSTA	651	TAATCAATCT	CAAGCAAAA CTGATTCTCT CAATGCTGCT TGTCTCAACT	700
MUSGLYTNS	651	TAATCAATCT	CAAGCAAAA CTAACTCTCT TGTCTGAT TGTCTCAACT	700
		Exon 4 ↓ Exon 5		
PGTCD	701	GTAATGCTTG	TGTTTTGGCA ATACATCAAC AGCCGAGAAG GTTCTTTCTT	750
BOVGSTA	701	GTCATTGTTG	TGTTTTGGCA ATATATCCAC AGCCGAGAAG GCTCTTTCTT	750
MUSGLYTNS	701	GTGCTTCTCG	TGTTTTGGCA ATATGTC AACCCGACAG GCTCTTTCTT	750
		Exon 5 ↓ Exon 6		
PGTCD	751	CTGCATATAC	CAGTCAAAA ACCCAGAACT TGGCAGCACT GGTCAAGGG	800
BOVGSTA	751	CTGCATATAAC	CCATCAAGAA ACCCAGAACT TGGTGGCAGC AGCAATTCAGA	800
MUSGLYTNS	751	CTGCATATAT	CACACAAAA TTGCAGAGCT TGGTCAAGAAC AGATGGCAGA	800
		Exon 6 ↓ Exon 7		
PGTCD	801	GCTGCTGG--	TTTCCGAGC TGGTTTAACTA ATGGCACTCA CAGTTACCAAC	850
BOVGSTA	801	AGGCTCTGTC	GCTTCCGACA TGGTTTAACTA ATG-----	850
MUSGLYTNS	801	AGCACTGGTG	GTTCCGAGC TGGTTTAAAA ATGGCACTCA CAGTTATCA	850
PGTCD	851	CAACAGCAAG	AGCTATACG CAACGAAAG CAACAAACAA AACAGACAA	900
BOVGSTA	851	CAACAGCATG	CACACATAAA CGAAGAAAG CAACAAACAA ACCAAGACAA	900
MUSGLYTNS	851	CAACAGCAAGC	TACAGGAGC CACACAAAA CGTACAAATG CAGATGGCAT	900
		Exon 7 ↓ Exon 8		
PGTCD	901	CACAGCAGAC	CTTCCGCTAG TGGACTGCTT TAATGCTGAG AAACGCCCCG	950
BOVGSTA	901	---AAGCAAG	CTTAAGCTAT CGGACTGCTT CAACCCATTT AAACGCCCCG	950
MUSGLYTNS	901	---TGAAGAC	CTCAGCTAT GGGACTGCTT CAATCCAAAG AAACGCCCCG	950
PGTCD	951	AGGCTGTGAC	CATAACCAGA TGGAAAGGCTC CAGTGGTATG GGAAGGCACT	1000
BOVGSTA	951	AGGTTGTGAC	CATGACCAAC TGGAAAGGCTC CAGTGGTATG GGAAGGCACT	1000
MUSGLYTNS	951	ATGTTTTCAC	ACTGACCCCG TGGAAAGGCTC CCATTGTCTG GGAAGGCACT	1000
PGTCD	1001	TACAACAGAG	CCGTCTTACA TAATTATAAT GCCAAGCAGA AAATTACCGT	1050
BOVGSTA	1001	TACAACAGAG	CCGTCTTACA CAATTATTAT GCCAAGCAGA AAATTACCGT	1050
MUSGLYTNS	1001	TATCAGACAG	CTCTGCTGCA AAAGTACTAC GCCACACAGA AACTCACTGT	1050
		Exon 8 ↓ Exon 9		
PGTCD	1051	GGCCTTGACC	CTTTTGGCTG TGGCAAGATA CATTGAGCAT TACTTGGAGG	1100
BOVGSTA	1051	GGCCTTGACC	CTTTTGGCTG TGGCAAGATA CATTGAGCAT TACTTGGAGG	1100
MUSGLYTNS	1051	GGCCTTGACA	CTTTTGGCTG TGGCAAGATA CATTGAGCAT TACTTAGAAG	1100
PGTCD	1101	AGTTCTTAAT	ATCTGCAAA ACATACTTCA TGGTGGGCA CAAGTCAATC	1150
BOVGSTA	1101	AGTTCTTAAC	GTCTGCTAAT AAGCACTTCA TGGTGGGCA CCACTCAATC	1150
MUSGLYTNS	1101	ACTTTCTGCA	GTCTGCTGAC ATCTACTTCA TGGTGGGCA TGGGCTCAAT	1150
PGTCD	1151	TTTTACATCA	TGGTGGATCA TATCTCCAGC ATGCCCTTCA TACAGCTGGC	1200
BOVGSTA	1151	TTTTATATCA	TGGTAGATCA TGTCTCCAGC ATGCCCTTCA TACAGCTGGC	1200
MUSGLYTNS	1151	TTTTACGTCA	TGATAGATCA CACCTCCCGC ATGCCCTGTC TGCACCTGAA	1200
PGTCD	1201	TGCTCTGGCC	TGCTTTAAAG TGTTCAGAT CAAGTCCGAC AAGAGCTGGC	1250
BOVGSTA	1201	TGCTCTGGCC	TGCTTTAAAG TGTTCAGAT CAAGCTCGAC AAGAGCTGGC	1250
MUSGLYTNS	1201	CCCTCTACAT	TGCTTTAAAG TGTTCAGAT CAAGCTCGAC AAGAGCTGGC	1250

POTCD	1251 AACACATCAG CATGATCCCG ATGAAGACCA TCGGGGACCA CATCGTGGCG	1300
BOVGSTA	1251 AGGACATCAG CATGATCCCG ATGAAGACTA TCGGGGACCA CATCGTGGCG	1300
MUSGLYTN	1251 AGGATATCAG CATGATCCCG ATGAAGACCA TTGGGGACCA CATCGTGGCG	1300
POTCD	1301 CACATCCAGC ACCAGCTTGA CTTCCTCTTC TGCATCCAGC TGCATCAGT	1350
BOVGSTA	1301 CACATCCAGC ATGAGCTTGA CTTCCTCTTC TGCATCCAGC TGCATCAGT	1350
MUSGLYTN	1301 CACATCCAGC ACCAGCTTGA CTTCCTCTTC TGCATCCAGC TGCATCAGT	1350
POTCD	1351 CTTCGAAAAC AACTTTGGCG TCGAGACCTT GGGGAGTGG GTCCCTCAGC	1400
BOVGSTA	1351 CTTCGAAAGC AACTTTGGCG TCGAGACCTT GGGGAGTGG GTCCCTCAGC	1400
MUSGLYTN	1351 CTTCGAAAGC AACTTTGGCG TCGAAACTCT GGGGAGCTG CTAGCCAGC	1400
POTCD	1401 TACAGGCGTG GTGGTAGAAG GCGATCCCTG ACCAGTTCAC CTAGCCAGC	1450
BOVGSTA	1401 TACAGGCGTG GTGGTAGAAG GCGATCCCTG ACCAGTTCAC CTAGCCAGC	1450
MUSGLYTN	1401 TCGAGGCGTG GTGGTAGAAG GCGATCCCTG ACCAGTTCAC CTATGAGC	1450
POTCD	1451 CGGAGCGAGT CGGAGCGCTA CATTCGCTTT CGGAGCGCG ATTTTATTA	1500
BOVGSTA	1451 CGGAGCGAGT CTGAGCGCTA CATTCGCTTC CGGAGCGCG ATTTTATTA	1500
MUSGLYTN	1451 CGGGAAGCTT CGGCGCGCTA CATTCGATTC CGGAGCGCG ATTTTACTA	1500
POTCD	1501 CCACCGAGCC ATTTTGGGG GAACAGCCAC TCAGGTCTTA AACATCAGC	1550
BOVGSTA	1501 CCATGCGAGC ATTTTGGGG GAACAGCCAC TCAGGTCTTT AACATCAGC	1550
MUSGLYTN	1501 CCACCGGCGC ATTTTGGGAC GAACCGCTAC TCACATTCTC AACCTCAGC	1550
POTCD	1551 AGGAGTCTTT CAGGGGAATC CTCCAGGACA AGGAAATGA CATAGAGCC	1600
BOVGSTA	1551 ACCATGCTTT CAAAGGAATC CTCAAGGACA AGAAATGA CATAGAGCC	1600
MUSGLYTN	1551 CGGAGTCTTT TAAGGGGATC CTCCAGGACA AGAAACATGA CATAGAGCC	1600
POTCD	1601 CACTGCCATC ATGAAGCCCA TCTAAACAG TATTTAATTC TCACAAAGC	1650
BOVGSTA	1601 CAATGCCATC ATGAAGCCCA TCTAAACAG TATTTCTTC TCACAAAGC	1650
MUSGLYTN	1601 CACTGCCATC ATCAGAGCCA CCTCAACAA TACTTCTTT TCACAAAGC	1650
POTCD	1651 CACTAAATC TTATCCCGC AATAGTCTG GCATTATCAT ATAGGCTGT	1700
BOVGSTA	1651 TACTAAATC TTATCCCGG AATAGTCTG GCATTATCAC ATAGGCTGT	1700
MUSGLYTN	1651 CACTAAATC CTATCTCGC AGTATTCTG GCACTATCAC ATAGGCTGT	1700
POTCD	1701 CTCTCCATAT TACCATCTC AAGATAGCTT GGCAGAAAA AGACTATAAT	1750
BOVGSTA	1701 CTCCGCAAT TAACTCTCT AAGATAGCTT GGCAGAAAA AGACTATAAT	1750
MUSGLYTN	1701 CTTCAGATAT TAAACTCTC AAGATAGCTT GGCAGAAAA AGACTATAAT	1750
POTCD	1751 TTGGTTAGAA ATAACATCTG AATTAAATTT GTCCAGCAG TTTCTCAAT	1800
BOVGSTA	1751 TTGGTTAGAA ATAATCTCTG ACTT-----T GTCCAGTAC ATTTCTCAAT	1800
MUSGLYTN	1751 TTGGTTAGAA ATAATCTCTG AATTCAATTT GTG----- --ATGGAAC	1800
POTCD	1801 TTCAAGAGT ATTACTCTGG CTACTTCTC ACAGAGTAG ---CACTTAA	1850
BOVGSTA	1801 TTCAAGAGT ATTATTCTGG CTACTTCTC ACAGAGTAG ---CACTTAA	1850
MUSGLYTN	1801 TTCAAC--T ATTACTCTGG CTAACTCTC AAACAAGTAG CAACACTTCA	1850

Stop

Fig. 4(cont) 4 - 4

PGTCD	1851	TTTTAACTTT	TAATAAATA	CTAACAAA-	----TACCAA	CACAGTAA-G	1900
BOVGSTA	1851	TTTTAACTTA	AAAAAATA	CTAACAAA-	----GACCAA	CACAGCAA-A	1900
MUSGLYTN	1851	TTTCAACTTT	TAAGAAG-A	CAATCAAAAC	CAAAACCCAC	TACCAATGCCA	1900
PGTCD	1901	TACATATTAT	TCTTCTTTC	AACCTTGAGC	CTTGTCAAA	GGCAGAAATCA	1950
BOVGSTA	1901	TACATATTAT	TCTTCTTTC	AACCTTGAGC	CTTGTAAATAC	GGCAGAAATCA	1950
MUSGLYTN	1901	AACAGATCAT	TCTTCTT-CA	CACCTTGAGC	CT-CTAAAT	GTCAAGAAACA	1950
PGTCD	1951	CTCTGTGC--	--TAATCAGA	TGTAAATTCC	CAGTCAATTC	2000
BOVGSTA	1951	ACCTGTGC--	--TAATCAGA	TGTAAATTCC	CAGTCAATTC	TTACCTAATTC	2000
MUSGLYTN	1951	CTCTATGCCA	AGTAATCAGG	TATAAATTCT	CAATCAATTC	TTACATATTC	2000
PGTCD	2001	2050
BOVGSTA	2001	TTCTTCTTCG	GGCCGGGGA	TGGATACACC	ATCAATTTGA	CT.....	2050
MUSGLYTN	2001	TGCTCTTTCG	GAAGAATTC	TTCTACAAAT	CAAAATTAAT	TTCAAGAAAGC	2050
PGTCD	2051	2100
BOVGSTA	2051	2100
MUSGLYTN	2051	AAAGCCACAT	GGCGGAACCT	TCTTCCCACT	CTGTCAATCA	ATTCAACCACT	2100
PGTCD	2101	2150
BOVGSTA	2101	2150
MUSGLYTN	2101	GGCCAGCTTC	TCAGAGAGCC	ATTAGCGAAC	AGTGTGCTTC	GTGTCAAGCT	2150
PGTCD	2151	2200
BOVGSTA	2151	2200
MUSGLYTN	2151	TGCAGCGCTC	CATCCCTTC	GCTTCATTA	CTTCTCTCTC	ATCGAATTC	2200
PGTCD	2201	2250
BOVGSTA	2201	2250
MUSGLYTN	2201	TAAAGCAAGC	CACAGAGCT	TTCCAGCCAC	ACACCTTTAA	TAAAGATCCG	2250
PGTCD	2251	2300
BOVGSTA	2251	2300
MUSGLYTN	2251	AATGTCAACA	TCAGTCTCTA	AAAGCTCATG	GCTCCAGCAG	CGCTGGCACT	2300
PGTCD	2301	2350
BOVGSTA	2301	2350
MUSGLYTN	2301	CCAGGCCCTCA	CTAGCTATT	GTCTCTCTCC	TCCGCATAA	GCAGCCACAG	2350
PGTCD	2351	2400
BOVGSTA	2351	2400
MUSGLYTN	2351	AGTCCCAATA	GTACTTTTC	TGCCACATGT	TCACAGTCCA	GGAAATATCA	2400
PGTCD	2401	2450
BOVGSTA	2401	2450
MUSGLYTN	2401	AGCTTCACCA	CTTACAGCCA	CATAGCACTT	GGGTTCTCTG	ATTCAACTCA	2450
PGTCD	2451	2500
BOVGSTA	2451	2500
MUSGLYTN	2451	GTACAAACA	CACAGAGCTT	TCTTCAGCAT	GACTAACACC	AGCAATTTGA	2500

Fig. 4(cont.) 4-5

PCTCD	2501	2550
BOVGSTA	2501	2550
MUSGLYTHS	2501	TGAAAGTGT	GTTCATTTC	TATTGCCAA	ATTGTATTCA	TGCTGTAGC
PCTCD	2551	2600
BOVGSTA	2551	2600
MUSGLYTHS	2551	TATGTGTGT	CAGCCCTGC	CAGAGGCTCT	CAGTGTATCA	GGGAGGACA
PCTCD	2601	2650
BOVGSTA	2601	2650
MUSGLYTHS	2601	GTACCTCAGC	GGACTCAGCA	CGAGCAGCCT	ATTATATCAG	AACACATCT
PCTCD	2651	2700
BOVGSTA	2651	2700
MUSGLYTHS	2651	CTCATCATCA	CGTCCCTACCT	ACAACCTGCT	CTGAGCTCC	CAGTCTCTCA
PCTCD	2701	2750
BOVGSTA	2701	2750
MUSGLYTHS	2701	GCCTATCTCT	TTCAGCTCTG	CGCCCTCTTA	TGCAGCAGCT	CAGTCAAGAC
PCTCD	2751	2800
BOVGSTA	2751	2800
MUSGLYTHS	2751	AAAGCCCTCT	GTACATCAGC	CTCATTTCCC	CTGCTCTAGT	ACTATGCLAG
PCTCD	2801	2850
BOVGSTA	2801	2850
MUSGLYTHS	2801	TGTGACAGCC	AGCCAGCCAG	ATGTACTGCA	CAACATAGCA	AGCCACTTCA
PCTCD	2851	2900
BOVGSTA	2851	2900
MUSGLYTHS	2851	TGGCATCTGG	AGCCGCACTC	ACTACAACCC	AGCTGCTCAA	CGTCTCTCTC
PCTCD	2901	2950
BOVGSTA	2901	2950
MUSGLYTHS	2901	CCCGCTCTCA	CAOCCTGCAG	CAGCCCTCTT	ATAAGCTGGT	CTCAAGCTAT
PCTCD	2951	3000
BOVGSTA	2951	3000
MUSGLYTHS	2951	GGCTGCGCAC	CCCTTTGCGA	AGTGTAAAT	GACCTTTTCA	CAGCTGTCCC
PCTCD	3001	3050
BOVGSTA	3001	3050
MUSGLYTHS	3001	CTAAGACCTT	TAAAAACAT	AGATATTTC	ACTCTGACTC	GTACAGTAG
PCTCD	3051	3100
BOVGSTA	3051	3100
MUSGLYTHS	3051	CAGATTTACA	GTATGAAAT	AGCAAGCGAA	ATAATTCTCC	CGTCTGTCTC

Fig 5

PBM Line-up (aa):

		Ex4 ↓ Ex5	Ex5 ↓ Ex6	
PCT(Frame 1)	1	MNVKGRVVL	MLVSTVMV	PHEYNSTEG SLFWIYQSKN PEVCGSAQR 50
BGT(Frame 1)	1	MNVKCKVIL	MLVSTVIW	PHEYNSTEG SLFWINPSRN PEVCGSSIQK 50
HGT(Frame 1)	1	MNVKCKVILL	MLIVSTVVV	PHEYNISTDC SLFWIYHTKI PEVGENRWQK 50
		Ex6 ↓ Ex7	Ex7 ↓ Ex8	
PCT(Frame 1)	51	GMWFPWFNN	GTHSYNEED	AIGNKXZQRK EDRGSLPLV DWFNPEKRP 100
BGT(Frame 1)	51	GMWLPWFNN	G---YKEEDG	DINEEKXQAN ED-ECXKLS DWFNPTKRP 100
HGT(Frame 1)	51	DWHPFSPFN	GTHGYQEDIV	EGRRK-GRN GDRIEEPQLW DWFNPKNRD 100
		Ex8 ↓ Ex9		
PCT(Frame 1)	101	AVTITRWKAP	VWECTYNRA	VLDNYHAKQK ITVGLTVFAV GRYSCHYLEZ 150
BGT(Frame 1)	101	VVTHTRWKAP	VWECTYNRA	VLDNYHAKQK ITVGLTVFAV GRYSCHYLEZ 150
HGT(Frame 1)	101	VLTVTPWKAP	IVWECTYDTA	LLEKYYATQK LTVGLTVFAV GXYIEHYLED 150
PCT(Frame 1)	151	FLISANTYFH	VGHXYIFYTH	VDDISRMPLI ELQPLASFKV FEIKSEKRWQ 200
BGT(Frame 1)	151	FLTSANKUHF	VGHPIVIFYTH	VDDISRMPLI ELQPLASFKV FEIKSEKRWQ 200
HGT(Frame 1)	151	FLESAENYFH	VGHVIFYTH	IDDTSRMPV HLNPLHSIQV FEIRSEKRWQ 200
PCT(Frame 1)	201	DISHMRKTI	GEHILAHIQH	EVDFLFCMDV DQVFQNNFGV ETLOQSVACL 250
BGT(Frame 1)	201	DISHMRKTI	GEHIVAHIQH	EVDFLFCMDV DQVFQDKFGV ETLOQSVACL 250
HGT(Frame 1)	201	DISHMRKTI	GEHILAHIQH	EVDFLFCMDV DQVFQDNFGV ETLOQLVACL 250
PCT(Frame 1)	251	QANWYKAPD	EFTYERRKES	AAIYIPFCQGD FYTHAAIFGG TPTQVLNITQ 300
BGT(Frame 1)	251	QANWYKADPH	DFTYERRKES	AAIYIPFCQGD FYTHAAIFGG TPTQVLNITQ 300
HGT(Frame 1)	251	QANWYKASPE	KFTYERRKES	AAIYIPFCQGD FYTHAAIFGG TPTHILNLTR 300
PCT(Frame 1)	301	ECFKGILQOK	ENDIEAQWHD	ESHLNKYLIL NKPTKILSPE YCHDYHIGMS 350
BGT(Frame 1)	301	ECFKGILQOK	KNDIEAQWHD	ESHLNKYFLL NKPTKILSPE YCHDYHIGLP 350
HGT(Frame 1)	301	ECFKGILQOK	KNDIEAQWHD	ESHLNKYFLL NKPTKILSPE YCHDYQIGLP 350
PCT(Frame 1)	351	VDIRIVKIAN	QKKEYNLVRN	NI*..... 400
BGT(Frame 1)	351	ADIXLVQMSH	QKKEYNLVRN	NV*..... 400
HGT(Frame 1)	351	SDIXSVKVAH	QKKEYNLVRN	NV*..... 400

Genetic map of the human $\alpha 1(I)$ collagen gene. The map shows a scale from 0 to 12 kb. Exons are represented by black boxes: exon 7 (approx. 10.5 kb), exon 8 (approx. 6.5 kb), and exon 9 (approx. 1.5 kb). Introns are represented by lines. Restriction enzyme sites are marked with vertical lines and labels: E (EcoRI), Sa (SmaI), B (BamHI), and SB (SmaI/BamHI). The map is labeled with $\lambda 1$, $\lambda 3$, $\lambda 7$, and $\lambda 5$. A legend indicates that black boxes represent exons and lines represent introns.

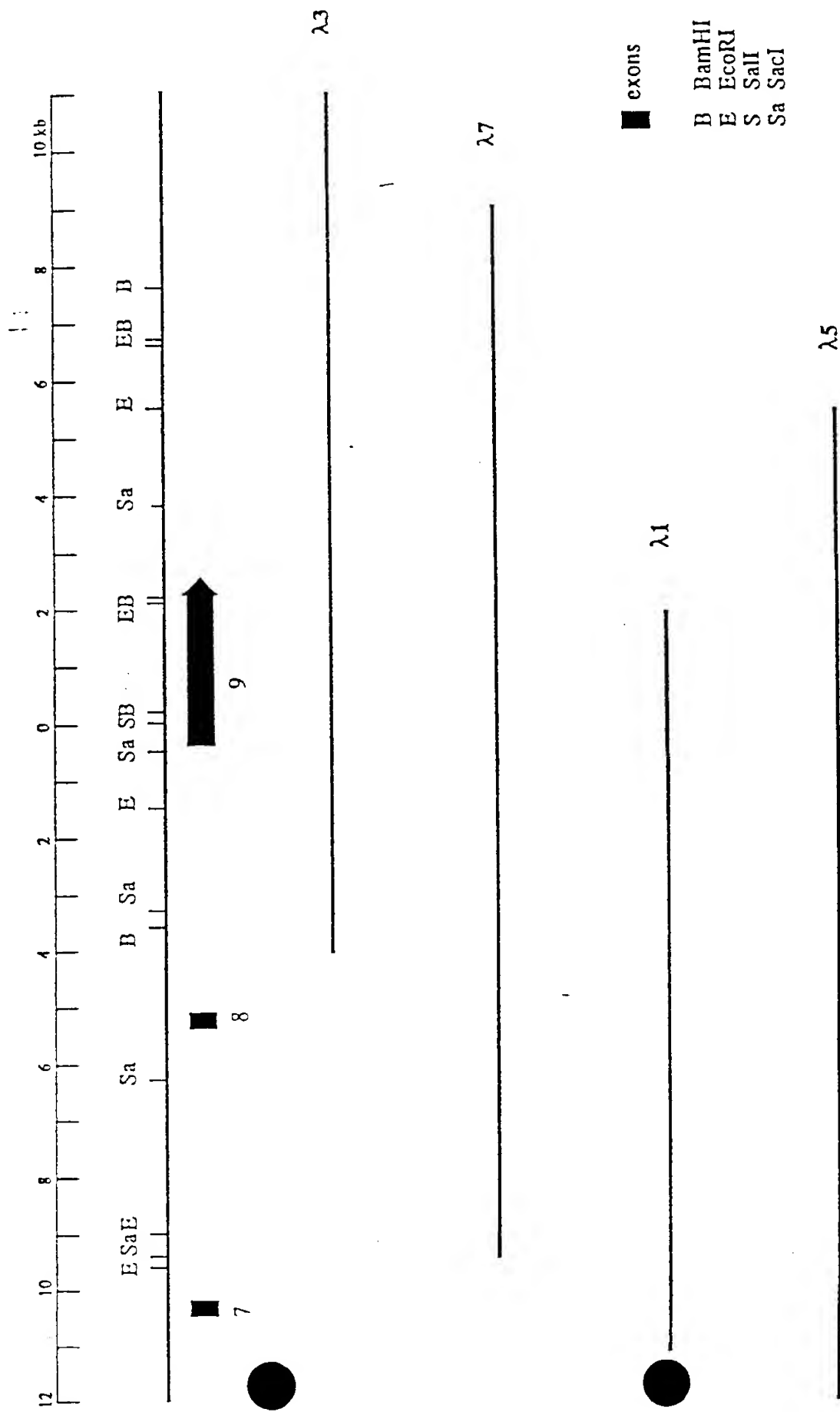
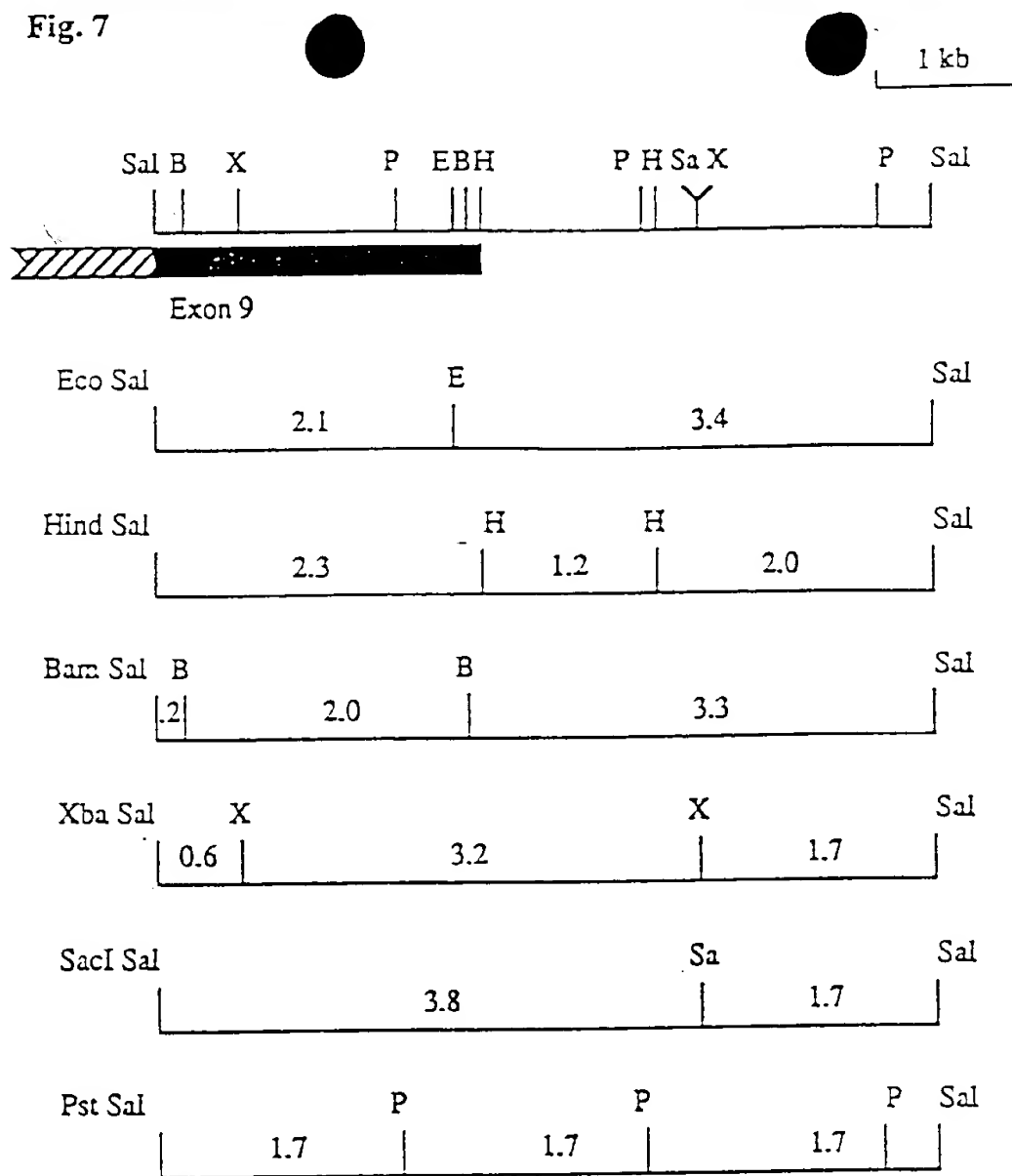


Fig. 7

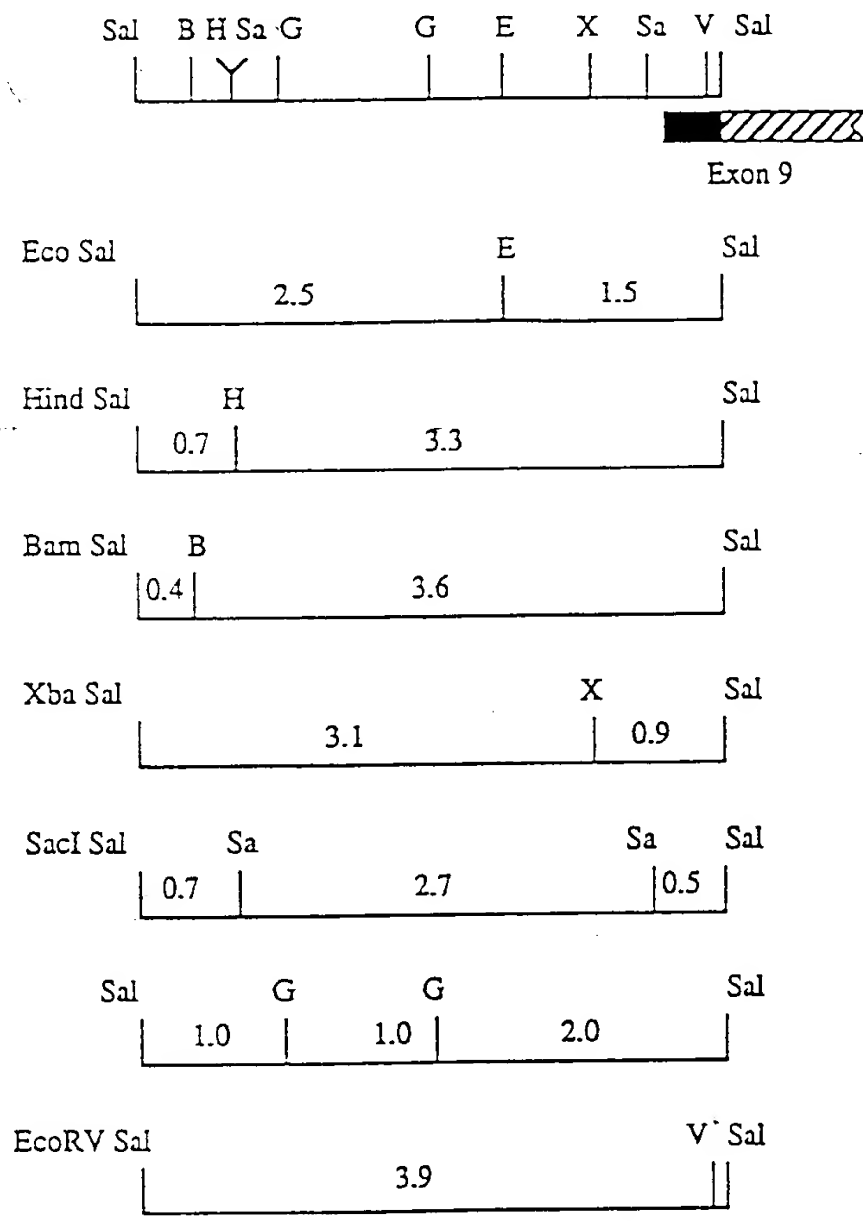


No sites for: BglII, Nde, PvuI, Xho, Kpn, SacII, EcoRV, Sma, Cla, Apa, Not

pBS+KS:

.... SacI SacII Not Xba Spe Bam Sma Pst Eco RV Hind Cla Sal Xho Apa Kpn





A ApaI
 B BamHI
 C ClaI
 E EcoRI
 G BglII
 H HindIII
 K KpnI
 N NotI
 P PstI
 S Sal
 Sa SacI
 V EcoRV
 X XbaI
 Xh XhoI

No sites for: Nde, PvuI, Xho, Kpn, SacII, Sma, Cla, Apa, Not

Unmapped sites for: Pst, PvuII

pUBS:

.... SacI SacII Not Xba Spe Bam Sma Pst Eco RV Hind Cla Sal Xho Apa Kpn



Fig. 9

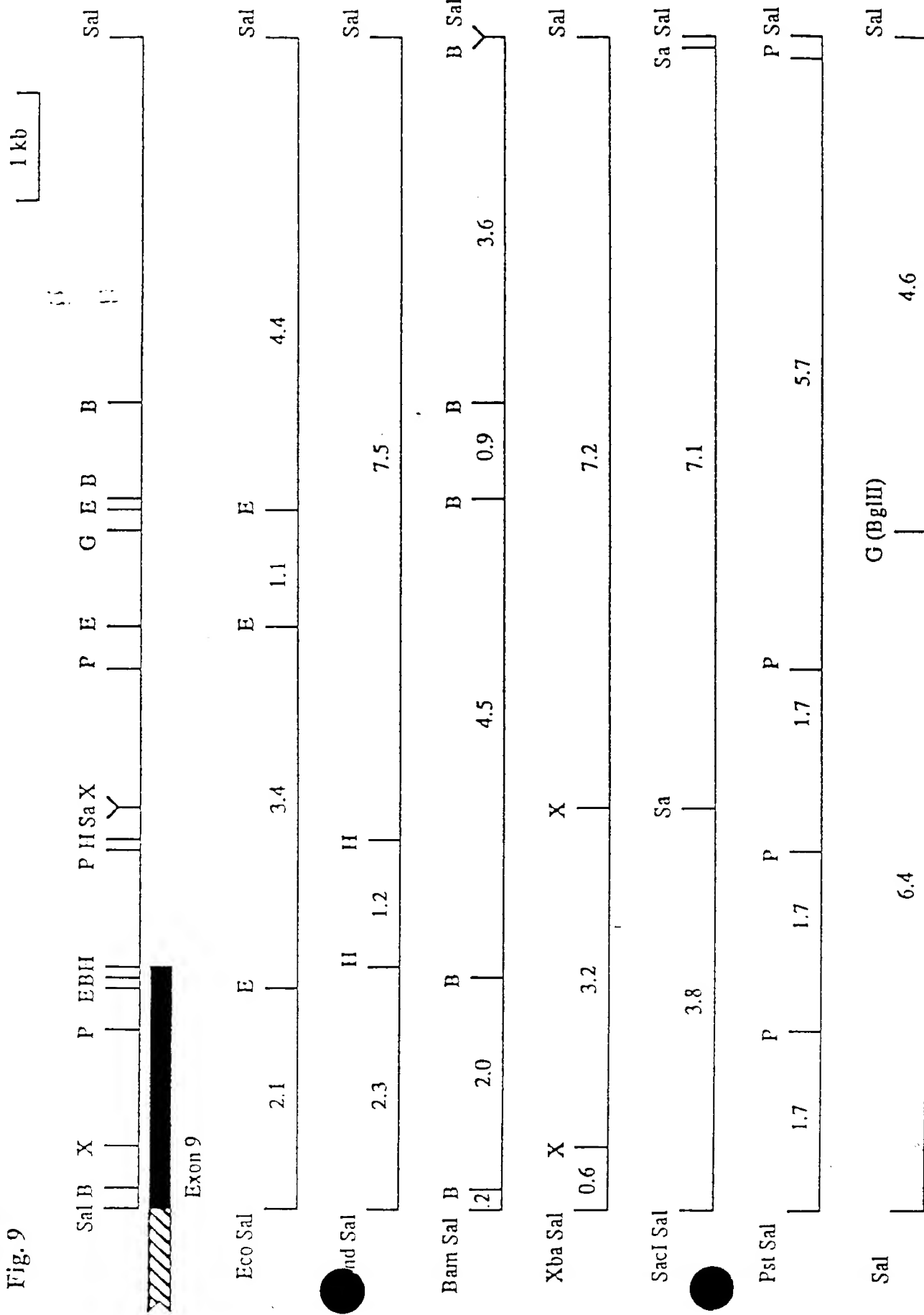


Fig. 9 (cont)

No sites for: Xho, Kpn, SacII, Sma, Cla, EcoRV, Apa, Not, PvuI, Nde

pUBS:

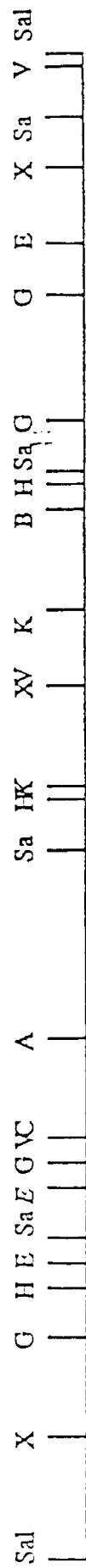
.... SacI SacII Not Xba Spe Bam Sma Pst Eco RV Hind Cla Sal Xho Apa Kpn



A	Apal
B	BamHI
C	ClaI
E	EcoRI
G	BglII
H	HindIII
K	KpnI
N	NotI
P	PstI
S	SalI
Sa	SacI
V	EcoRV
X	XbaI
Xh	XhoI

Fig. 10

1 kb



Exon 9

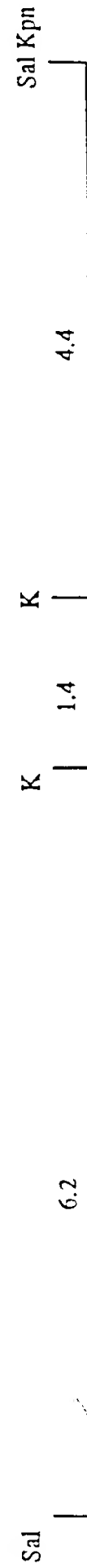
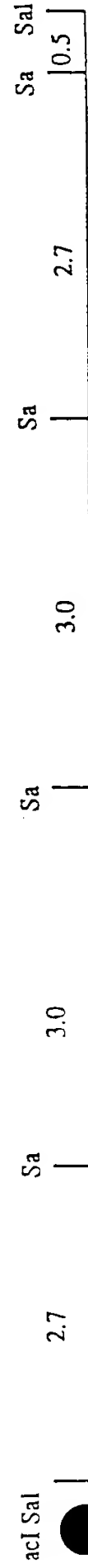
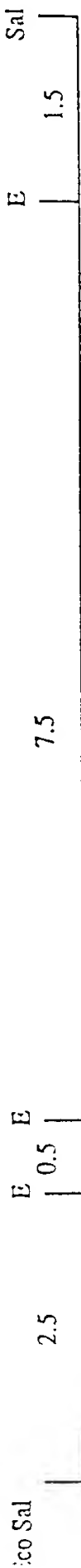
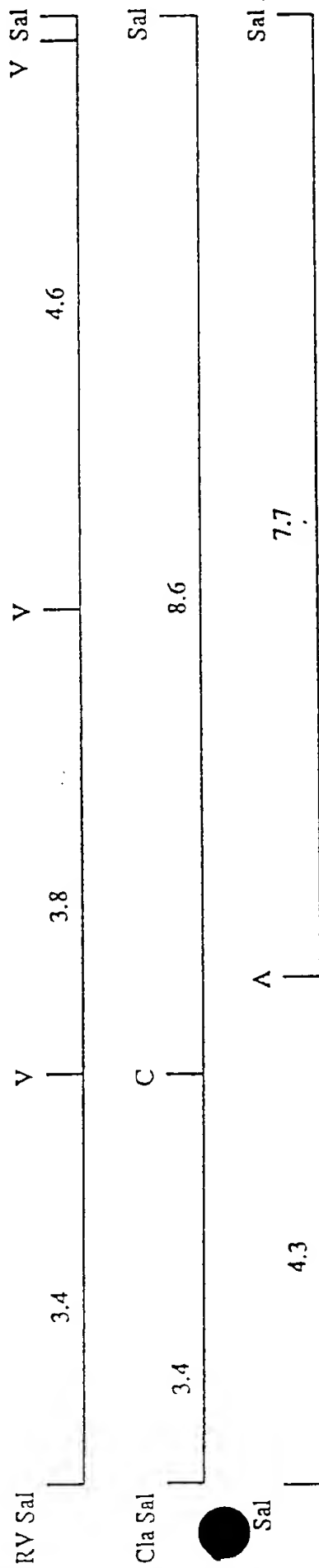


Fig. 10 (cont)



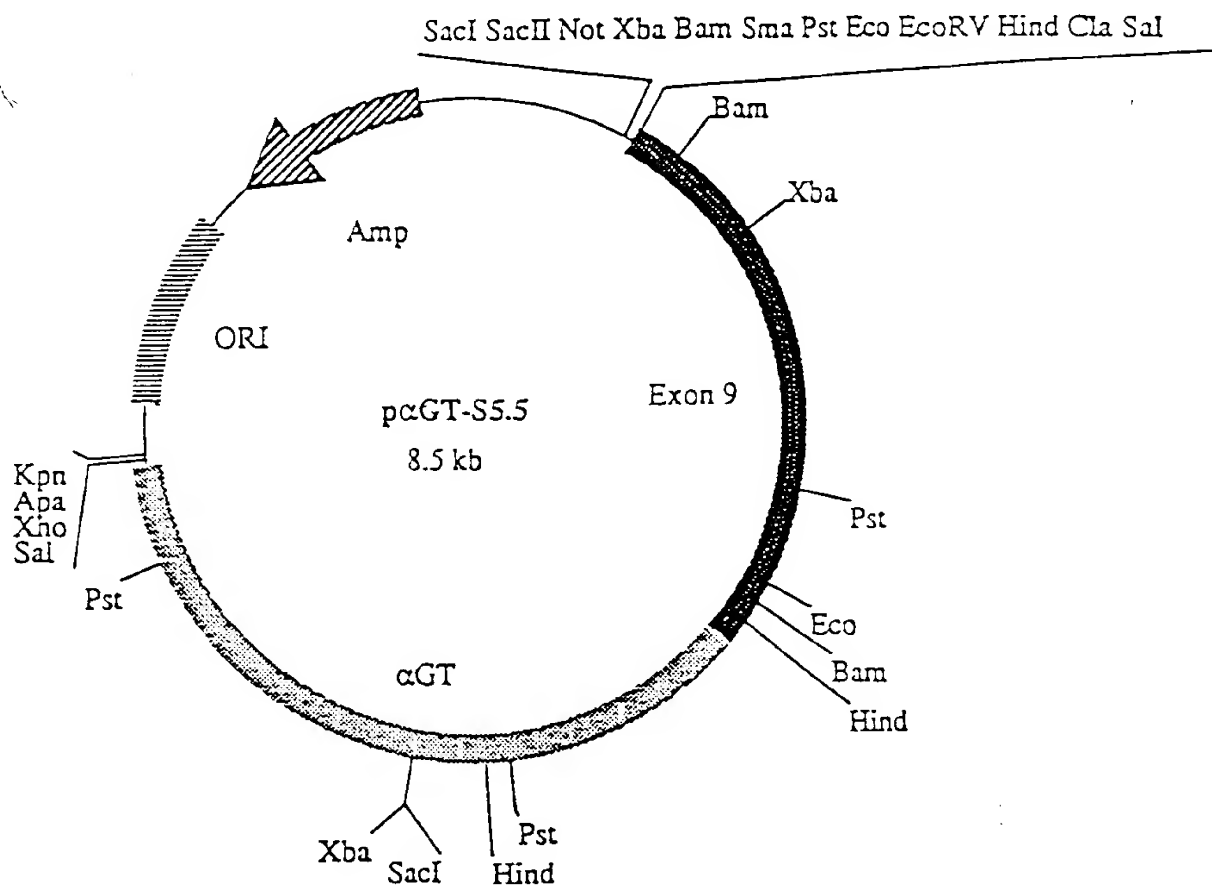
No sites for: Xho, SacII, Sma, Not






pUBS:

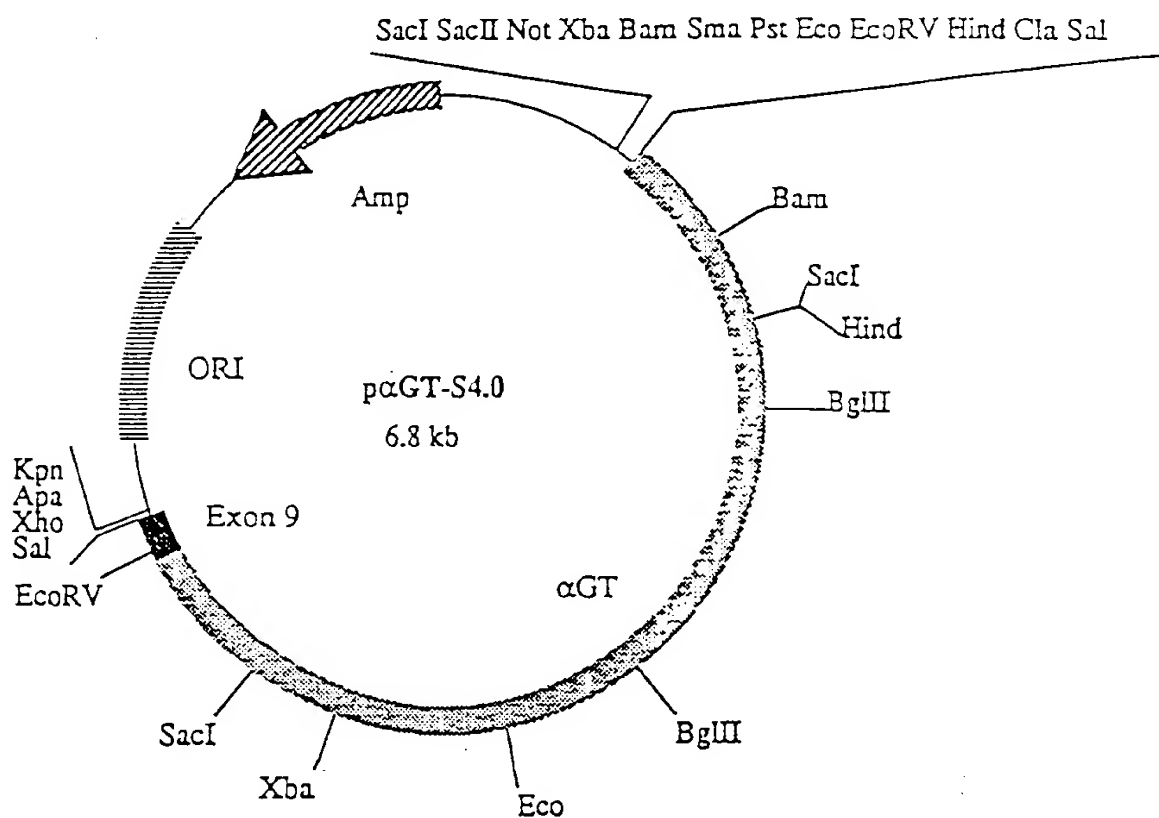
.... SacI SacII Not Xba Spe Bam Sma Pst Eco RV Hind Cla Sal Xho Apa Kpn








A ApaI
B BamHI
C ClaI
E EcoRI
G BglII
H HindIII
K KpnI
N NotI
P PstI
S Sal
Sa SacI
V EcoRV
X XbaI
Xh XhoI

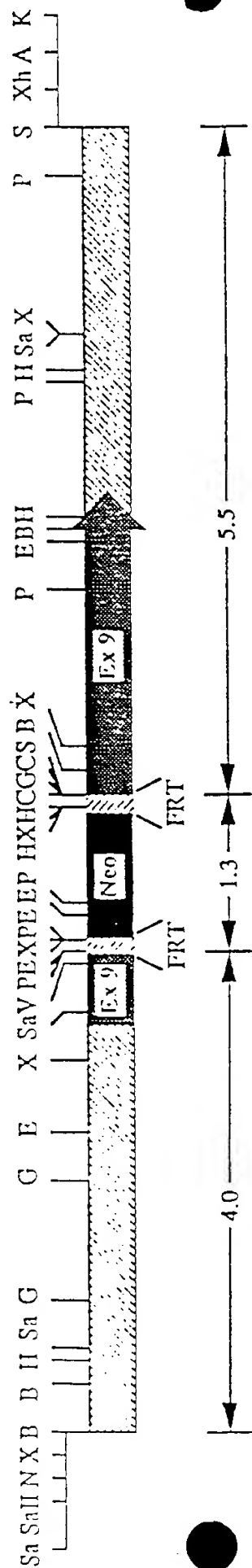


-  α1,3 galactotransferase (αGT) non-coding DNA
-  Exon 9 of αGT
-  Neo resistance gene
-  Bacterial origin of replication
-  Amp resistance gene

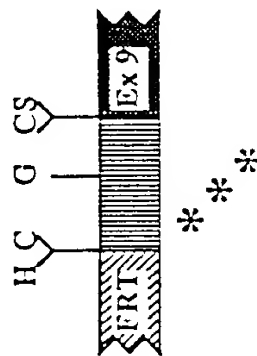









-  α1,3 galactotransferase (αGT) non-coding DNA
-  Exon 9 of αGT
-  Neo resistance gene
-  Bacterial origin of replication
-  Amp resistance gene

ig. 13



region around Cla-Bgl linker



-  α 1,3 galactotransferase (α GT)
-  non-coding DNA
-  Exon 9 of α GT
-  Neo resistance gene
-  FRT recombination site
-  Cla-Bgl linker
-  Stop codons

- A ApaI
- B BamHI
- G ClaI
- H EcoRI
- K BglII
- N HindIII
- P KpnI
- S NotI
- Sa PstI
- V SalI
- X SacI
- Xh EcoRV
- X XbaI
- Xh XhoI

Fig. 14

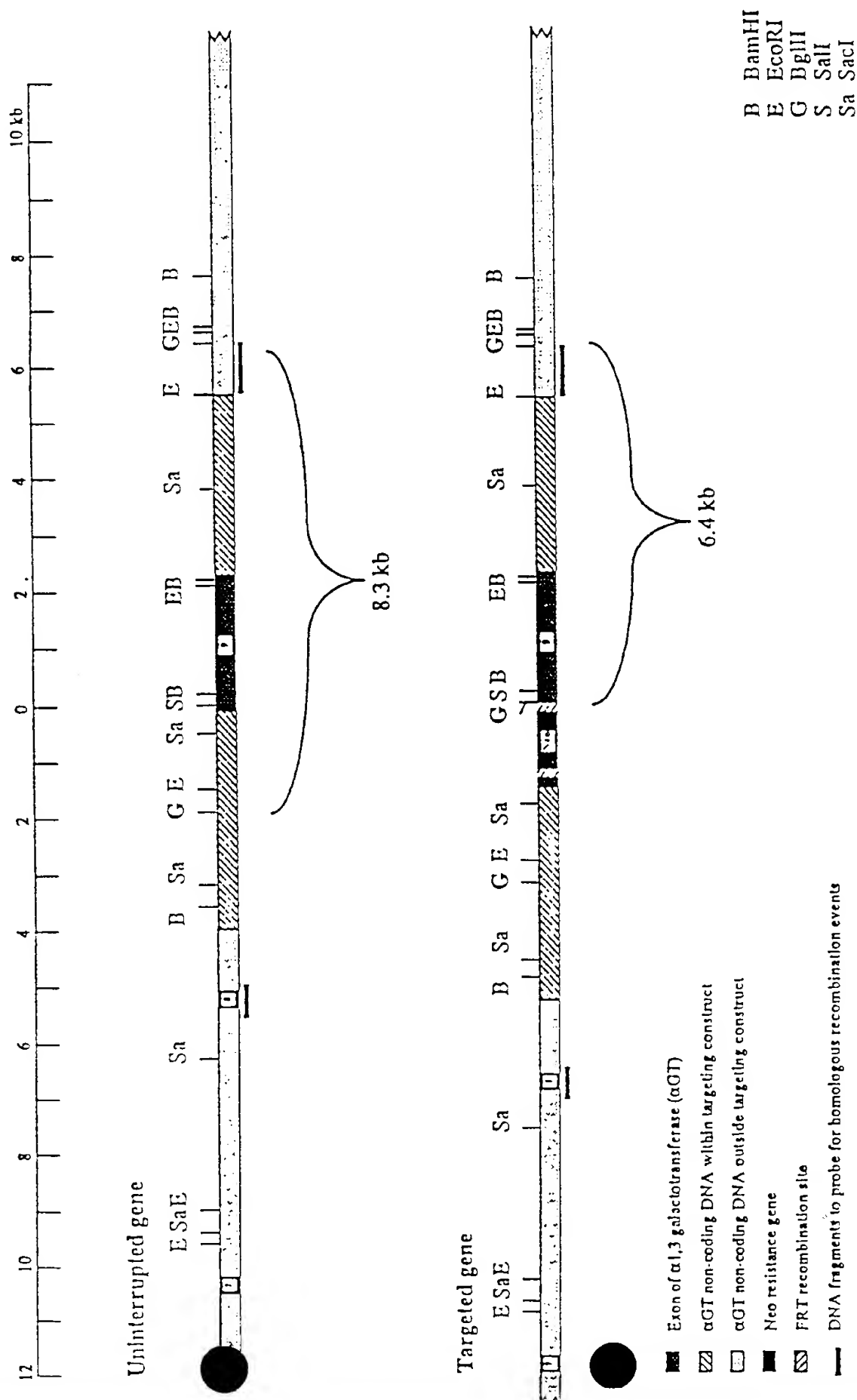


Fig. 15

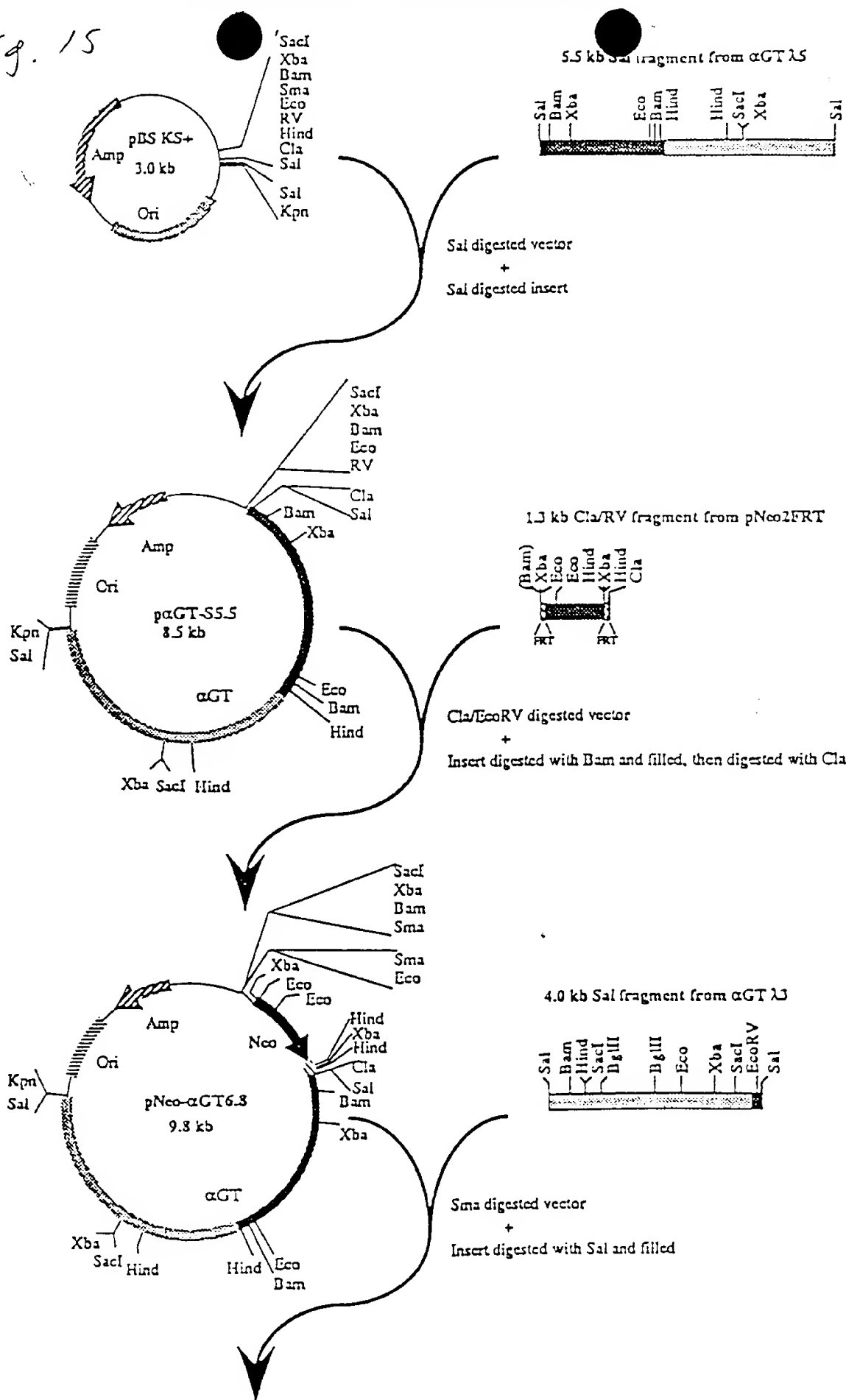


Fig. 16

10	20	30	40	50	60
GAGGGCTGCA	GGAAATTCGAT	GATCCCCCAG	CTTGAAGTTC	CTATTCCGAA	GTTGCTATTC
70	80	90	100	110	120
TCTAGAAAGT	ATAGGAACTT	CAAGCTGGGC	TGCAGGAATT	CGATTCCGAGC	AGTGTGGTTT
130	140	150	160	170	180
TGCAAGAGGA	AGCAAAAAGC	CTCTCCACCC	AGGCCTGGAA	TGTTTCCACC	CAATGTCCAG
190	200	210	220	230	240
CAGTGTGGTT	TTGCAAGAGG	AAGCAAAAAG	CCTCTCCACC	CAGGCCTGGA	ATGTTTCCAC
250	260	270	280	290	300
CCAATGTGCA	GCAAACCCCG	CCCAGCGTCT	TGTCAATTGGC	GAATTCCGAC	ACCCAGATCC
310	320	330	340	350	360
AGTGGGGGGG	GGGGGGTCCC	AGGTCCACTT	GGCATATTAA	GGTGACGGGT	GTGGGCTGGA
370	380	390	400	410	420
ACACCGAGCG	ACCGTGCAGC	CAATATGGGA	TCCGGCATTC	AACAAGATGG	ATTGCCAGCA
430	440	450	460	470	480
GGTGTCCCGG	CCGCTTGGGT	GGAGAGGCTA	TTCCGGTATG	ACTGGGCACA	ACAGACATC
490	500	510	520	530	540
GGGTGCTCTG	ATGGCGCGGT	GTTCCGGGCTG	TCAGCGCAGG	GGCGCCCGGT	TCTTTTGTTC
550	560	570	580	590	600
AAGACCGACC	TGTCCGGTGC	CCTGAATGAA	CTCCAAGAGC	AGGCAGCGCG	GCTATCGTGG
610	620	630	640	650	660
CTGGCCACGA	CGGGCGTTCC	TTGGCCAGCT	GTGCTCGAGC	TTGTCACTGA	AGCGGGAAGG
670	680	690	700	710	720
GACTGGCTGC	TATTCGGGCA	AGTGGCGGGG	CAGGATCTCC	TGTCACTGCA	CCTTGCCTCT
730	740	750	760	770	780
GGCGAGAAAG	TATCCATCAT	GGCTGATGCA	ATGCGGCGGC	TGCATACGCT	TGATCCGGCT
790	800	810	820	830	840
ACCTGCCCCAT	TCGACCACCA	AGCGAAACAT	CGCATCGAGC	GAGCACCTAC	TCCGATGGAA
850	860	870	880	890	900
GGCGGTCTTG	TCGATCAGGA	TGATCTGGAC	GAAGAGCATC	AGGGGCTGGC	GGCAGCCGAA
910	920	930	940	950	960
CTGTTCGCCA	GGCTCAAGGC	GGGGATGCCC	GACGGCGAGG	ATCTCGTCTG	GACCCATGGC
970	980	990	1000	1010	1020
GATGCCCTGCT	TGCCGAATAT	CATGGTGGAA	AATGGCGCGT	TTTCTGGATT	CATCGACTGT
1030	1040	1050	1060	1070	1080
GGCCGGCTGG	GTGTGGCGGA	CCGCTATCAG	GACATAGCGT	TGGCTACCGG	TGATATTGCT
1090	1100	1110	1120	1130	1140
GAAGAGCTTG	GCGGCGAATG	GGCTGACCGC	TTCTCTGTGC	TTTACGGTAT	CGCCGCTCCC
1150	1160	1170	1180	1190	1200
GATTCCGAGC	GCATCGCCTT	CTATCGCCTT	CTTGACGAGT	TCTTCTGAGG	GGATCGGCAA
1210	1220	1230	1240	1250	1260
TAAAAAGACA	GAATAAAACG	CACGGGTGTT	GGCGGTTTGT	TCCGATCATC	AAGCTTGAAG

Fig. 16 (cont)

1270	1280	1290	1300	1310	1320
TTCTATTCC	GAAGTTCCTA	TTCTCTAGAA	AGTATAGGAA	CTTCAAGCTT	ATCGATGAGT
1330	1340	1350	1360	1370	1380
AGATCTTGAT	CGATACCGTC

Linker sequences : 0-28

FRT : 29-104

Polyoma virus enhancer repeats : 105-249

Herpes Simplex Virus Tyrosine Kinase promoter : 250-385

Neomycin phosphotransferase coding region : 385-1188

Herpes Simplex Virus Tyrosine Kinase PolyA signal : 1189-1249

FRT : 1250-1310

Linker sequences : 1311-1340

Fig. 17

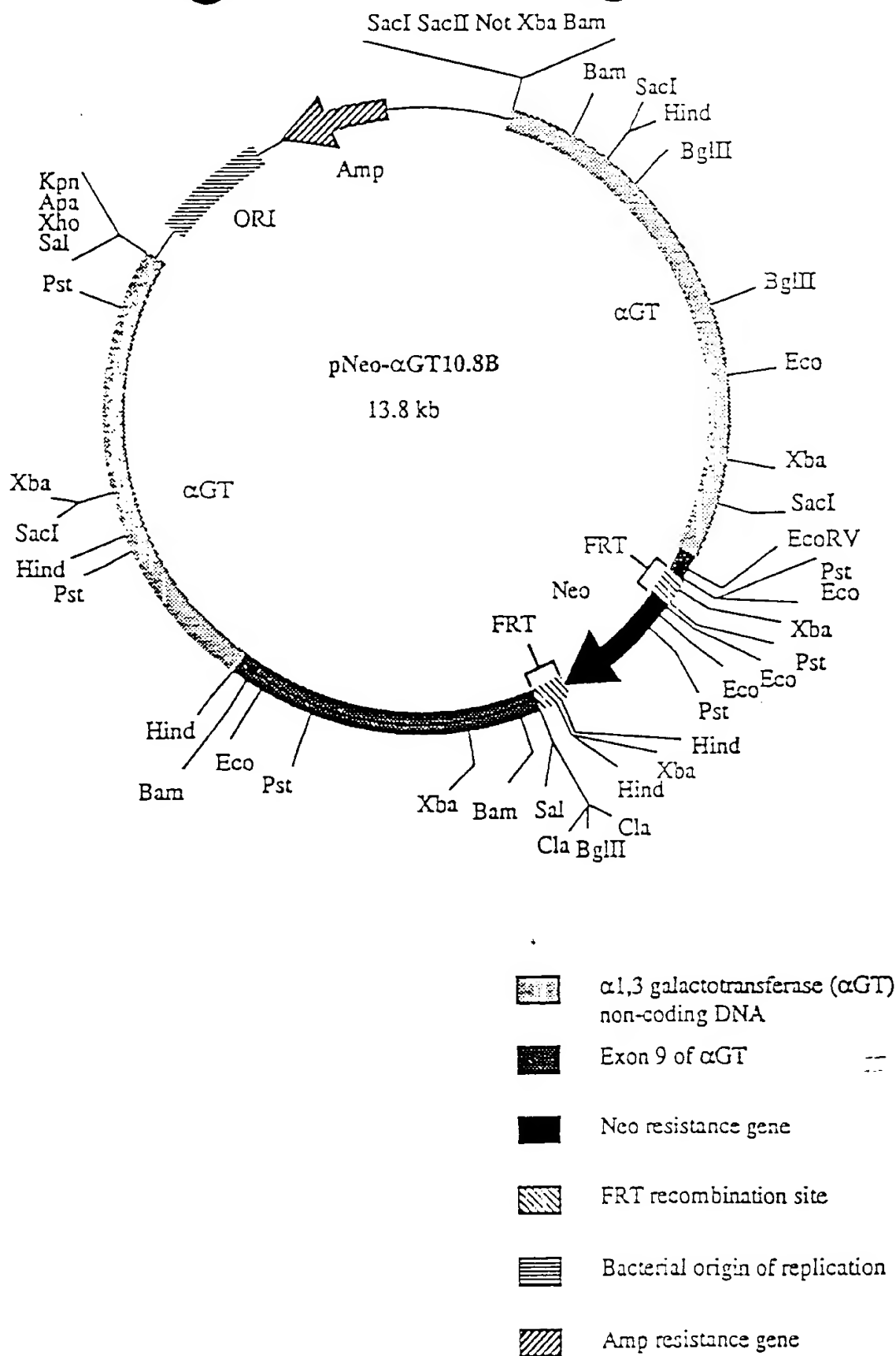
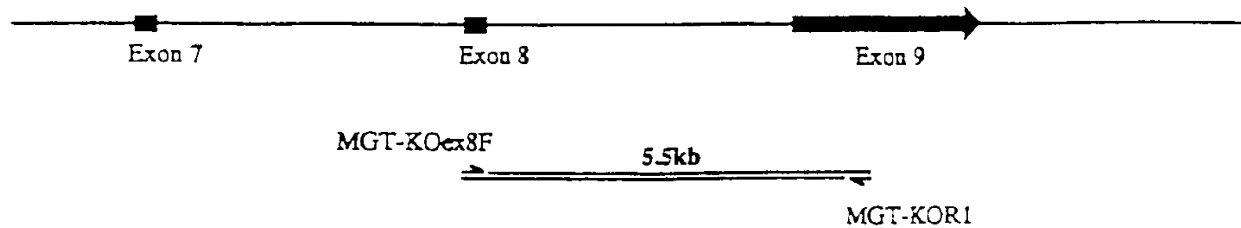


Fig. 17

Uninterrupted gene



Targeted gene

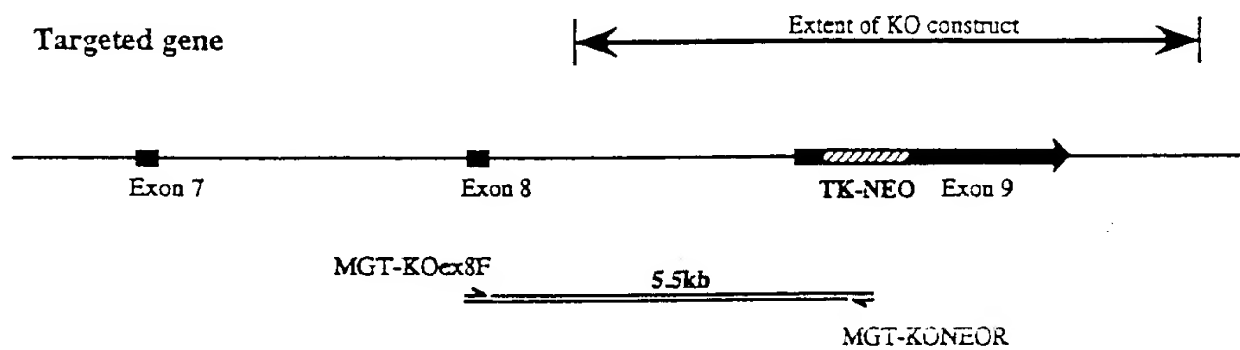
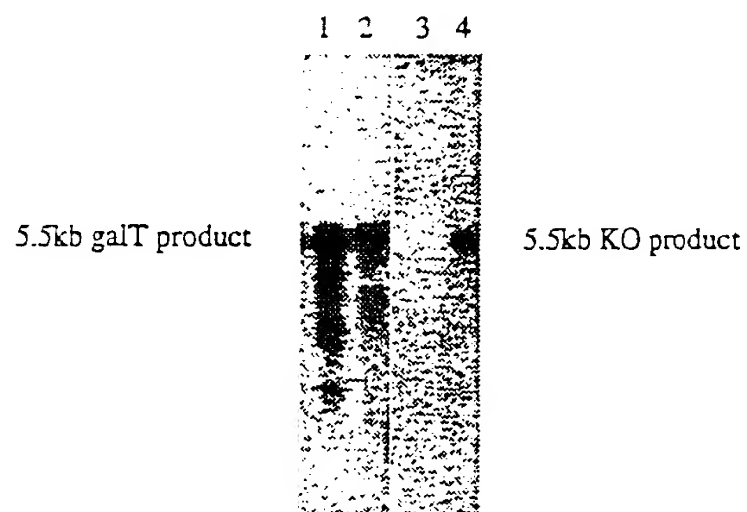


Fig. 18



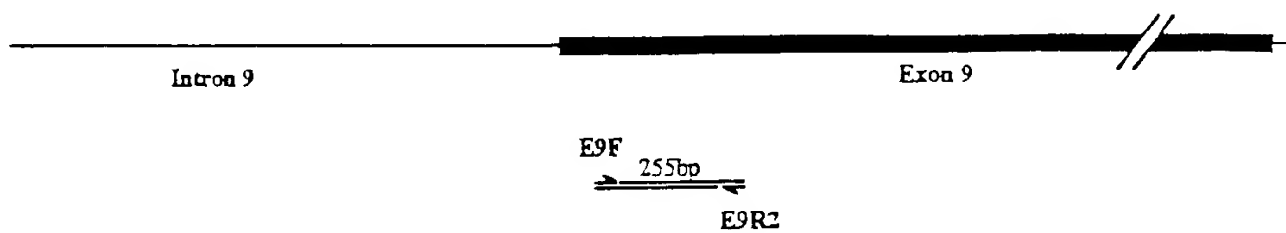
Fig.



1. CBAC template; wild type primers
2. 7C2 template; wild type primers
3. CBAC template; KO primers
4. 7C2 template; KO primers

Fig. 21

Uninterrupted gene



Targeted gene

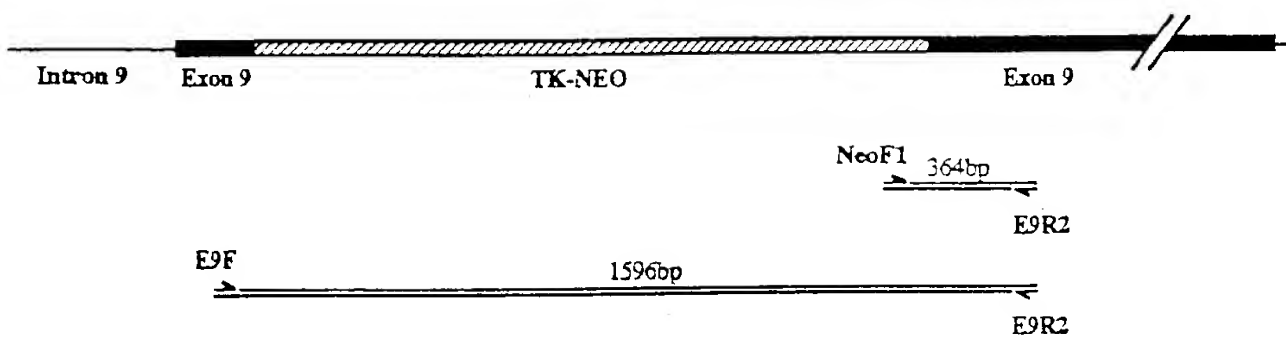


Fig. 22

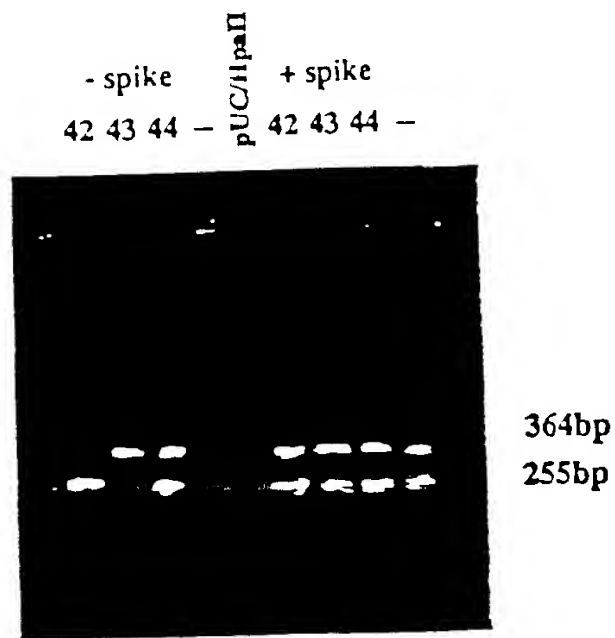
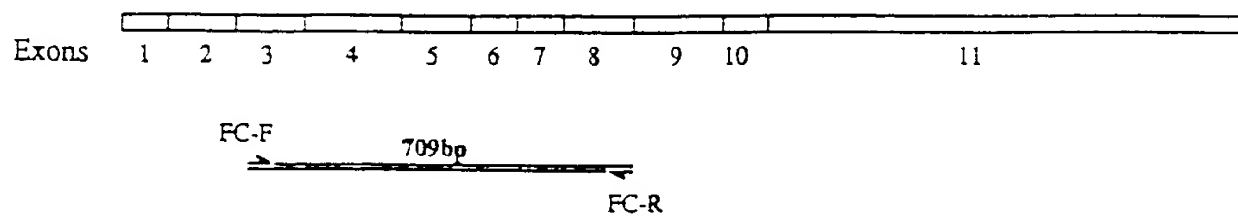
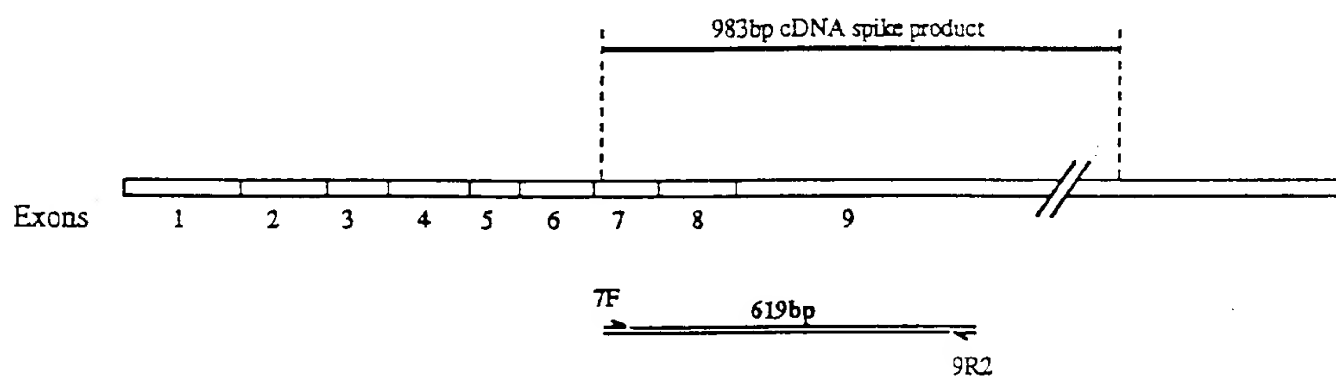


Fig. 23

Primer binding sites within mouse ferrochelatase cDNA

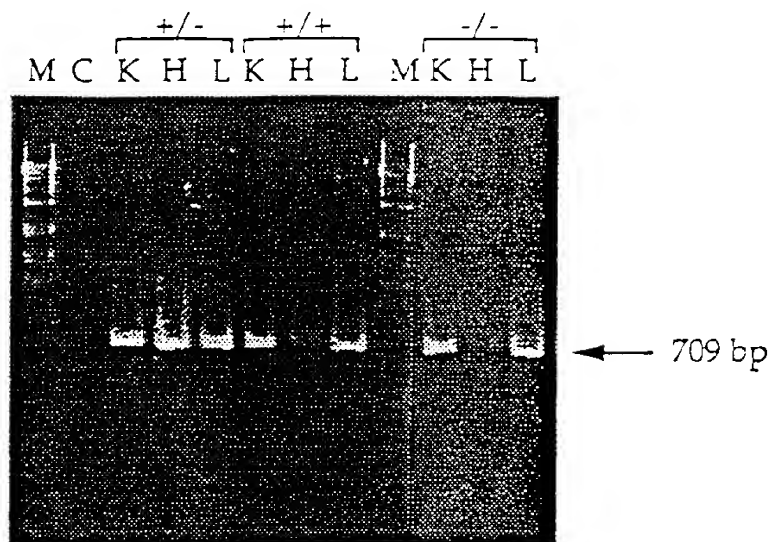


Primer binding sites within mouse α -1,3-GalT cDNA

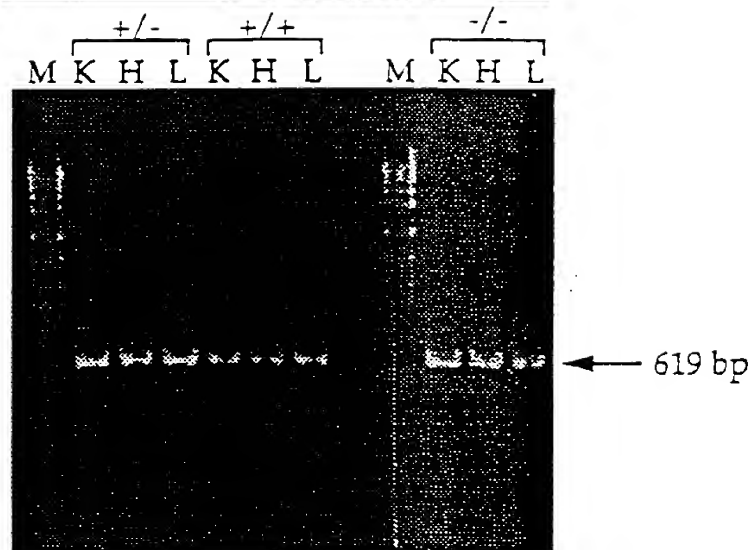


i) Ferrochelatase, FC-F/R

M, Marker SPP-I
C, MQW control
K, KIDNEY
H, HEART
L, LIVER



ii) α -1,3-GT cDNA spike
+ 7F/9R2 primers



iii) α -1,3-GT 7F/9R2 primers

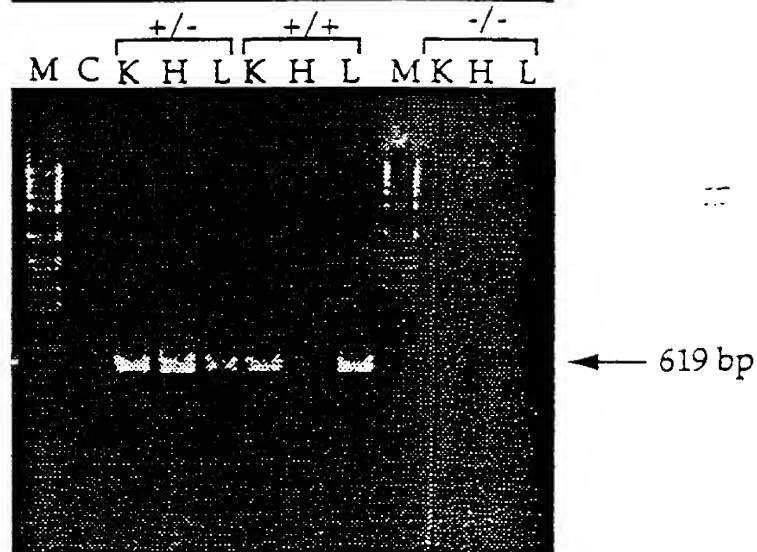
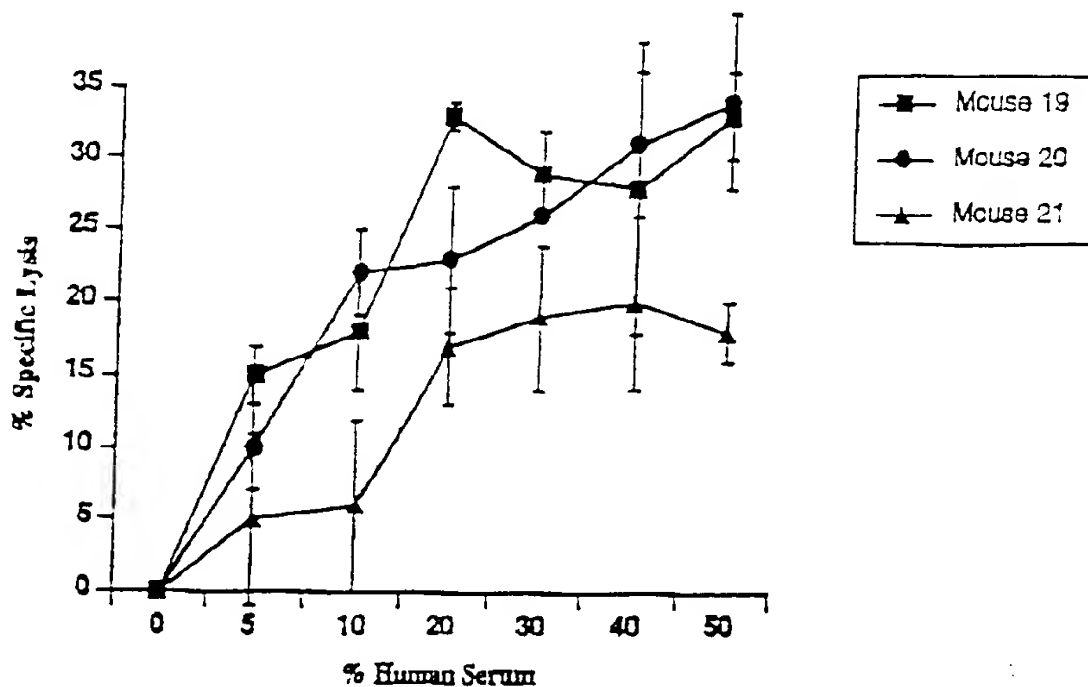


Fig. 25



Mouse 19: Wild type; Mouse 20: Heterozygote Gal KO; Mouse 21:
Homozygous Gal KO

Fig. 26

T-LIF SEQUENCE - Murine

CTGACACCTTTGCGTTTCCTCTTGGGTGTCCGGCTGCGACCTTTCCCCACCCC
GGCCTCTTTCCCTGGTTGCACCACTTCCTCTCATTCCAAAGGATTGTGCCCTTA
CTGCTGCTGGTTCTGCACTGGAAACACGGGGCAGGGAGCCCTCTTCCCATCAC
CCCTGTAAATGCCACCTGTGCCATACGCCACCCATGCCACGGCAACCTC

Met	Asn	Gln	Ile	Lys	Asn	Gln	Leu	Ala	Gln	Leu	Asn	Gly	
ATG	AAC	CAG	ATC	AAG	AAT	CAA	CTG	GCA	CAG	CTC	AAT	GGC	
Ser	Ala	Asn	Ala	Leu	Phe	Ile	Ser	Tyr	Tyr	Thr	Ala	Gln	Gly
AGC	GCC	AAT	GCT	CTC	TTC	ATT	TCC	TAT	TAC	ACA	GCT	CAA	GGX
Glu	Pro	Phe	Pro	Asn	Asn	Val	Glu	Lys	Leu	Cys	Ala	Pro	Asn
GAG	CCG	TTT	CCC	AAC	AAC	GTG	GAA	AAG	CTA	TGT	GCG	CCT	AAC
Met	Thr	Asp	Phe	Pro	Ser	Phe	His	Gly	Asn	Gly	Thr	Glu	Lys
ATG	ACA	GAC	TTC	CCA	TCT	TTC	CAT	GGC	AAC	GGG	ACA	GAG	AAG
Thr	Lys	Leu	Val	Glu	Leu	Tyr	Arg	Met	Val	Ala	Tyr	Leu	Ser
ACC	AAG	TTG	GTG	GAG	CTG	TAT	CGG	ATG	GTC	GCA	TAC	CTG	AGC
Ala	Ser	Leu	Thr	Asn	Ile	Thr	Arg	Asp	Gln	Lys	Val	Leu	Asn
GCC	TCC	CTG	ACC	AAT	ATC	ACC	CGG	GAC	CAG	AAG	GTC	CTG	AAC
Pro	Thr	Ala	Val	Ser	Leu	Gln	Val	Lys	Leu	Asn	Ala	Thr	Ile
CCC	ACT	GCC	GTG	AGC	CTC	CAG	GTC	AAG	CTC	AAT	GCT	ACT	ATA
Asp	Val	Met	Arg	Gly	Leu	Leu	Ser	Asn	Val	Leu	Cys	Arg	Leu
GAC	GTC	ATG	AGG	GGC	CTC	CTC	AGC	AAT	GTG	CTT	TGC	CGT	CTG
Cys	Asn	Lys	Tyr	Arg	Val	Gly	His	Val	Asp	Val	Pro	Pro	Val
TGC	AAC	AAG	TAC	CGT	GTG	GGC	CAC	GTG	GAT	GTG	CCA	CCT	GTC
Pro	Asp	His	Ser	Asp	Lys	Glu	Ala	Phe	Gln	Arg	Lys	Lys	Leu
CCC	GAC	CAC	TCT	GAC	AAA	GAA	GCC	TTC	CAA	AGG	AAA	AAG	TTG
Gly	Cys	Gln	Leu	Leu	Gly	Thr	Tyr	Lys	Gln	Val	Ile	Ser	Val
GGT	TGC	CAG	CTT	CTG	GGG	ACA	TAC	AAG	CAA	GTC	ATA	AGT	GTG
Val	Val	Gln	Ala	Phe	***								
GTG	GTC	CAG	GCC	TTC	TAG	AGAGGAGGTCTTGAATGTACCATGGACTG...							

Fig. 27

HUMAN T-LIF SEQUENCE

GACCTTTTGC CTTTCTCTC TCCTGGTGCA CCATTTCCTC TCCCTCCCTG	50
AGCCGGAGTT GTGCCCCTGC TGTGGTTCT GCACTGGAAA CATGGGGCGG	100
GGAGCCCCCT CCCCATCACC CCTGTCAACG CCACCTGTGC CATAAGCCAC	150
CCATGTCACA ACAACCTC ATG AAC CAG ATC	182
Met Asn Gln Ile	
AGG AGC CAA CTG GCA CAG CTC AAT GGC AGT GCC AAT GCC CTC	227
Arg Ser Gln Leu Ala Gln Leu Asn Gly Ser Ala Asn Ala Leu	
5 10 15	
TTT ATT CTC TAT TAC ACA GCC CAG GGG GAG CCG TTC CCC AAC	272
Phe Ile Leu Tyr Tyr Thr Ala Gln Gly Glu Pro Phe Pro Asn	
20 25 30	
AAC CTG GAC AAG CTA TGT GGC CCC AAC GTG ACG GAC TTC CCG	317
Asn Leu Asp Lys Leu Cys Gly Pro Asn Val Thr Asp Phe Pro	
35 40 45	
CCC TTC CAC GCC AAC GGC ACG GAG AAG GCC AAG CTG GTG GAG	362
Pro Phe His Ala Asn Gly Thr Glu Lys Ala Lys Leu Val Glu	
50 55 60	
CTG TAC CGC ATA GTC GTG TAC CTT GGC ACC TCC CTG GGC AAC	407
Leu Tyr Arg Ile Val Val Tyr Leu Gly Thr Ser Leu Gly Asn	
65 70	
ATC ACC CGG GAC CAG AAG ATC CTC AAC CCC AGT GCC CTC AGC	452
Ile Thr Arg Asp Gln Lys Ile Leu Asn Pro Ser Ala Leu Ser	
75 80 85	
CTC CAC AGC AAG CTC AAC GCC ACC GCC GAC ATC CTG CGA GGC	497
Leu His Ser Lys Leu Asn Ala Thr Ala Asp Ile Leu Arg Gly	
90 95 100	
CTC CTT AGC AAC GTG CTG TGC CGC CTG TGC AGC AAG TAC CAC	542
Leu Leu Ser Asn Val Leu Cys Arg Leu Cys Ser Lys Tyr His	
105 110 115	
GTG GGC CAT GTG GAC GTG ACC TAC GGC CCT GAC ACC TCG GGT	587
Val Gly His Val Asp Val Thr Tyr Gly Pro Asp Thr Ser Gly	
120 125 130	
AAG GAT GTC TTC CAG AAG AAG AAG CTG GGC TGT CAA CTC CTG	632
Lys Asp Val Phe Gln Lys Lys Lys Leu Gly Cys Gln Leu Leu	

Fig. 27 (cont.) 27-2

	135	140	
GGG AAG TAT AAG CAG ATC ATC GCC GTG TTG GCC CAG GCC TTC			677
Gly Lys Tyr Lys Gln Ile Ile Ala Val Leu Ala Gln Ala Phe			
145	150	155	
TAG CAGGAGGTCT			722

Fig. 28

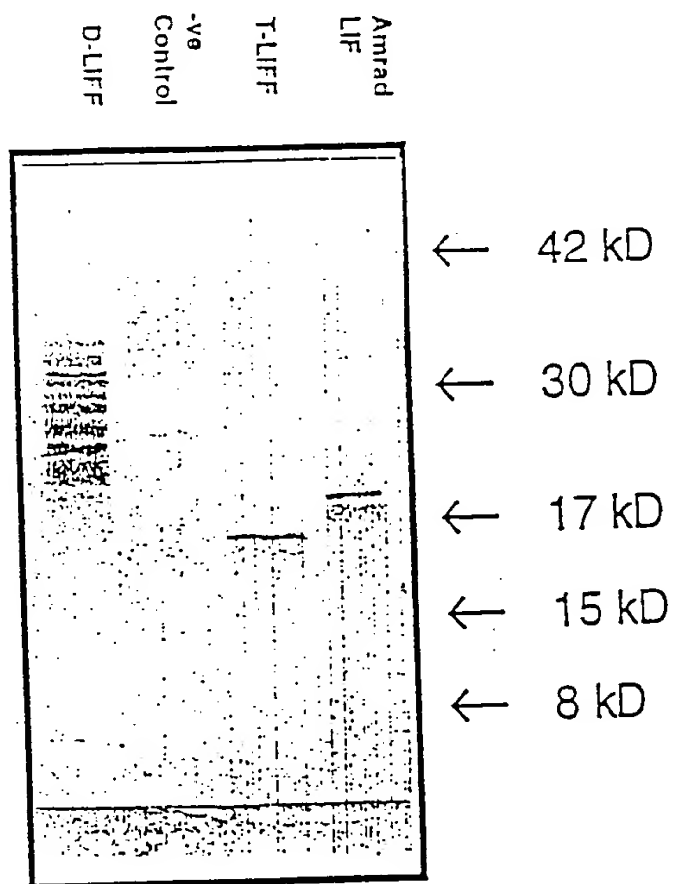
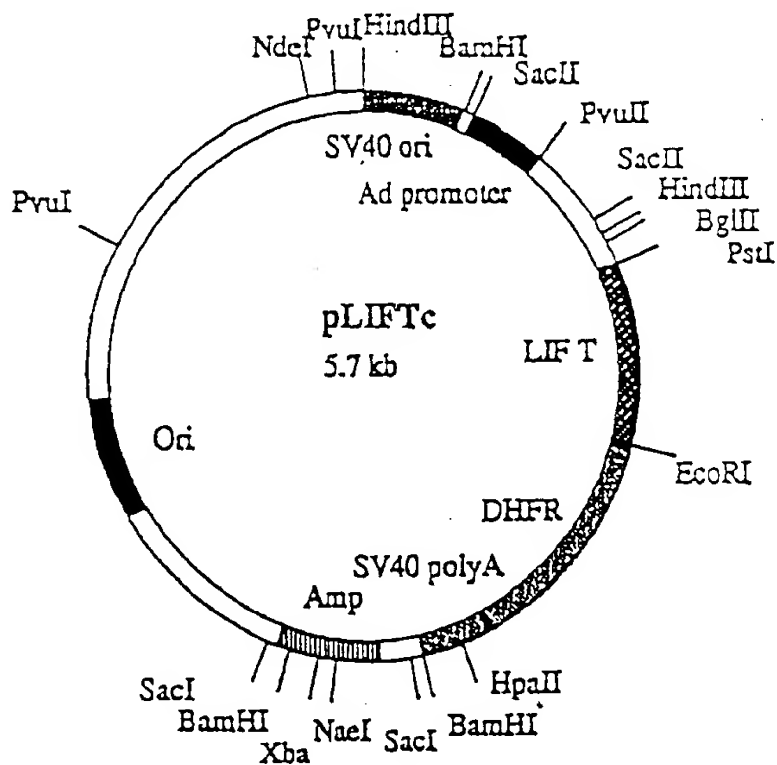


Fig. 29

(30)









-  SV40 origin of replication
-  Adenovirus promoter
-  LIF T coding region
-  Dihydrofolate reductase 3' end
-  Ampicillin resistance gene
-  Bacterial origin of replication

Fig. 30

